

REMARKS

The official action of 9 June 2009 has been carefully considered and reconsideration of the application as amended is respectfully requested.

Independent claims 115 and 141 have been amended in accordance with the description in the specification as filed at, for example, paragraphs [0036] and [0064].

Specifically, paragraph [0036] describes the dosage that is released by irradiation of a selected element and paragraph [0064] identifies the iodine in the rose bengal as the selected element that is irradiated to cause the emission of Auger electrons in the described dose. See, also, original claims 118-120. The amendment to the claims removes the basis for the rejection under 35 USC 112, second paragraph appearing on pages 2-3 of the official action.

The claims stand rejected as allegedly being unpatentable over Cash et al in view of Wang and Ariel et al. Applicants respectfully traverse this rejection.

First, Applicants respectfully note that, in responding to the arguments in Applicants' Amendment filed 9 April 2009, the Examiner did not address Applicants main argument, namely: the cited art does not provide a **reasonable expectation of success**. The prior art can be modified or combined to reject claims as *prima facie* obvious only so long as there is a **reasonable expectation of success**. See MPEP 2143.02. In the present action, the Examiner has contended that there is a motivation to combine the cited references, but has not explained why there would have been a reasonable expectation of success. As discussed below, the cited art would not have provided even a reasonable expectation that the claimed dosage could be used to provide for the preferential destruction of tumor cells in a subject while localizing the damage so as not to severely injure a patient. In the absence of such reasonable expectation of success, the cited art is incompetent to set forth even a *prima facie* case of obviousness for

the invention as claimed.

As discussed in Applicants Amendment filed 9 April 2009, the claimed invention is based at least in part upon Applicants' discovery that, with the use of bright x-ray beams of defined line emissions tuned to the absorption edge of a selected element (iodine) in rose bengal, it is possible to cause the emission of Auger electrons from rose bengal accumulated in the lysosomes of irradiated cells in a dose of at least 10^6 Gy within a few atomic distances from iodine in the rose bengal. This causes the disruption of the lysosomes and death of the cells containing such lysosomes (specification at paragraph [0063]), while localizing the damage to such cells (specification at paragraph [0065] and [0038]).

This is explained in detail in the Declaration under 35 USC 1.132 of Dr. C.G. Wang filed 9 April 2009. As discussed in the declaration, rose bengal accumulates within the lysosomes of cells and the Auger electrons from an Auger cascade caused by irradiating the cells with line emission x-rays tuned to the K-absorption edge of iodine deliver 10^6 Gray in a very small ionization sphere. This sphere of damage is so localized (a few atomic distances) that it would be harmless everywhere in a cell except the DNA and the lysosomes in the cell. Thus, the Auger cascade can be used to destroy the cells by flooding the cytoplasm of the cells with HCl from the lysosomes without destroying other cells outside of the very small ionization sphere.

In contrast, the primary reference, Cash et al, teaches the use of heavy elements as X-ray intensifiers but does not show or suggest the use of line emission x-rays to cause emission of Auger electrons from the iodine in rose bengal accumulated in the lysosomes of cells in a dose of at least 10^6 Gy within a few atomic distances from iodine in the rose bengal whereby to cause disruption of the lysosomes and death of the irradiated cells without destroying surrounding cells. In fact, insofar as Cash et al teach the necessity of limiting the dose of radiation used in the method described therein, they teach away from a method which generates a dose of at least 10^6 Gy. See Cash et al at, e.g., column 12, lines 43-48 (“a preferred approach is to irradiate the patient 10 so that the tumor receives 1600 cGy in a single dose, and the surrounding healthy tissue receives 1600/de cGy.”); see, also, column 15, Example 1 (“At the skin, a dose of 10 Gy accumulates, which is **too high for healthy skin.**” Emphasis added.)

There is nothing in the reference which shows or suggests that the generation of Auger electrons of at least 10^6 Gy, as required in the claimed method, would be localized so as to prevent damage to normal tissue outside of a tumor to which irradiation is applied. In the absence of such teaching, the reference could not provide even a reasonable expectation of success with the claimed method.

The secondary references cited by the Examiner cannot supplement the deficiencies in the primary reference. In particular, Wang do not show or suggest the use of line emission x-rays tuned to the K- or L- absorption edge of rose bengal to create an

Auger cascade that can be used selectively to destroy tumor cells **without destroying healthy tissue**. Moreover, the primary reference teaches away from the need to tune x-rays to the K-edge of iodine. See Cash et al at column 6, lines 63-67 ("Iodine (I, element 53), a common element in contrast media, has its K-edge at 33.2 keV. At this low energy, x-rays penetrate only a short distance into the body, so x-ray sources are mostly configured to operate at energies above 34 keV, and there is no issue of tuning to the element."); see, also, Cash et al at column 9, lines 33-39. Finally, none of the cited references teaches that rose bengal accumulates in the lysosomes of cells such that the irradiation of iodine in the rose bengal can be used to turn the lysosomes in a cell into a therapeutic apparatus.

In view of the above, Applicants respectfully submit that the prior art rejection and all other rejections and objections of record have been overcome and that the application is now in allowable form. An early notice of allowance is earnestly solicited and is believed to be fully warranted.

Respectfully submitted,

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